

Left atrial and left ventricular diastolic function during acute myocardial ischaemia

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Abstract

Objective—To study indices of diastolic left ventricular function during the first few seconds of myocardial ischaemia.

Design—Isovolumic and total relaxation times and left atrial and left ventricular dP/dt were identified from high fidelity (micromanometer) pressure recordings in the left ventricle and left atrium during percutaneous transluminal angioplasty of the left anterior descending coronary artery.

Patients—20 patients with isolated disease of the left anterior descending artery and normal left ventricular function.

Results—The isovolumic relaxation time lengthened during the first seven to nine seconds of ischaemia; then it shortened by an average of 15% up to the twentieth second, initially as a result of increased left atrial contractility and subsequently because of impaired ventricular relaxation. Ventricular ischaemia resulted in impaired left ventricular diastolic compliance, as shown by an increase in the total relaxation time, before there was evidence of systolic impairment. Minimum dP/dt decreased progressively (by -37% at the twentieth second of ischaemia), whereas maximum dP/dt fell only after 20 seconds of ischaemia (by -11%).

Conclusions—Relaxation and filling of the left ventricle (indices of diastolic function) are more sensitive to myocardial ischaemia than myocardial contractility and systolic function. Left atrial contractility increases during left ventricular ischaemia.

(Br Heart J 1992;68:377-81)

The physiology of left ventricular diastole is complex and the determinants of left ventricular filling are poorly understood. In the absence of aortic regurgitation or a defect of the interventricular septum, left ventricular filling begins at the onset of mitral valve opening and ends with mitral valve closure. Diastolic transmitral blood flow is determined by the interrelation of active left ventricular relaxation, chamber compliance, atrial contraction, and venous return from the pulmonary circulation. A tripartite mechanism of normal left ventricular filling has been described: a rapid filling phase that begins immediately after mitral valve opening and lasts about

200 ms, followed by a period of slow filling or diastasis, the duration of which is dependent on the heart rate. Left ventricular filling during sinus rhythm finishes with left atrial contraction.^{1,2}

Although myocardial ischaemia is known to increase the left ventricular filling pressure (left ventricular end diastolic pressure) its effect on this tripartite mechanism has not been well characterised and in humans cannot be studied in the setting of myocardial infarction or spontaneously occurring angina pectoris. In an earlier paper we described the use of controlled myocardial ischaemia of the anterior left ventricular wall during angioplasty of the left anterior descending coronary artery (LAD) to study the effects of ischaemia on left atrial function.³ In this study we used the same model to investigate the effect of segmental left ventricular ischaemia on the separate determinants of left ventricular filling (active relaxation, chamber stiffness, and left atrial contraction).

Patients and methods

PATIENTS

We studied 20 patients (16 men and four women) aged 40-71 (mean 49) years during elective coronary angioplasty. All patients had stable angina pectoris of effort and were in sinus rhythm. Diagnostic coronary arteriography had shown significant disease of the proximal left anterior descending artery (LAD) with a reduction of luminal diameter of $\geq 75\%$ (estimated by the operator) and no other significant coronary disease. Patients with a collateral supply to the LAD territory were excluded from the study. All patients had normal left ventricular function at rest, and none had disease of either the aortic or mitral valves. None had a defect of the interventricular septum.

The procedure was approved by the hospital ethics committee and written informed consent was obtained in advance from each patient. All patients were given premedication with diazepam (10 mg), nifedipine (10 mg), and aspirin (500 mg). Routine antianginal agents were stopped at least 24 hours before the angioplasty was performed.

Methods

We used the femoral approach for cardiac catheterisation. A double micromanometer catheter with 5 cm between the sensors (Millar PC 771) was introduced into the left

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Accepted for publication
15 April 1992

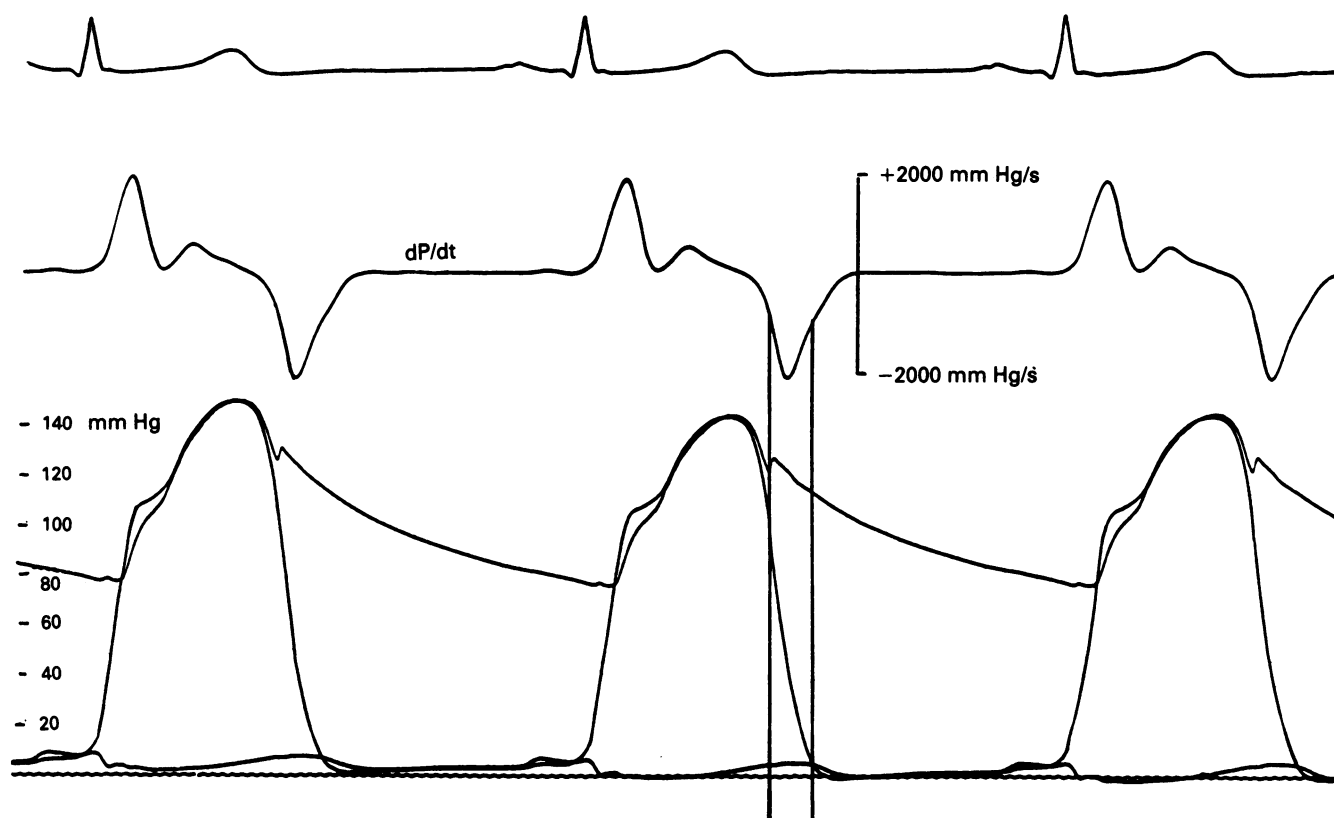


Figure 1 Simultaneous recordings of the electrocardiogram; left ventricular dP/dt ; and micromanometer aortic, left ventricular, and left atrial pressures. The notch on the left atrial trace coincided with aortic valve closure; the parallel vertical lines indicate the isovolumic relaxation time (interval from aortic valve closure to the crossover of left ventricular and left atrial pressures).

heart by the transseptal route; the distal pressure sensor was located in the left ventricle and the proximal sensor in the left atrium. All patients were given intravenous heparin (10 000 units) once transseptal puncture had been performed. An 8F left coronary artery guiding catheter was positioned from the right femoral artery. In five patients a 7F pigtail catheter was inserted retrogradely into the left ventricle from the left femoral artery.

The micromanometers were calibrated electronically against a mercury manometer before insertion. Simultaneous recordings of left ventricular and left atrial pressure and the first order derivatives with respect to time (dP/dt) of left ventricular pressure were made on photographic paper and on digital tape. Left atrial and left ventricular pressures were monitored continuously during LAD angioplasty, which was performed with a conventional co-axial dilatation system. Balloon inflation was maintained for 20–30 seconds and repeated up to five times until a satisfactory angiographic result had been obtained. In five patients, bi-plane left ventricular angiography was performed before angioplasty and during the first 5–10 seconds of balloon inflation.

The duration of the isovolumic relaxation time (the interval from aortic valve closure to mitral valve opening) was used as an index of active left ventricular relaxation. As has been shown previously, it is possible to identify aortic valve closure from a vibration on the high fidelity left atrial pressure trace, which coincides with the dicrotic notch in the aortic

pressure trace.³ The isovolumic relaxation time was measured from simultaneously recorded high fidelity traces of the left ventricular and left atrial pressures as the interval from the vibration of aortic valve closure in the left atrial trace to the crossover of the left ventricular–left atrial pressure tracings. “Total relaxation time” was calculated from aortic valve closure to the nadir of the left ventricular pressure curve during diastole (fig 1).

Assessment of a change in left ventricular stiffness arising from acute ischaemia was made by analysis of regional left ventricular wall motion, before and during balloon inflation in the LAD. Left atrial function before and during acute ventricular ischaemia was assessed by analysis of the left atrial pressure trace.

Changes from control values were assessed by a paired t test (5% level of significance).

Results

The table lists the haemodynamic indices as means (SD). The heart rate increased slightly during balloon inflation from the control value of 72 (6) beats/min; the increase was statistically significant by the twentieth second of inflation (77 (9) beats/min ($p < 0.05$)). Left ventricular systolic pressure did not change during the first seven seconds of ischaemia, but had declined by 11% at the end of 14 seconds from 149 (12) mm Hg to 132 (14) mm Hg ($p < 0.05$). At the end of 20 seconds it had fallen

Table Effects of balloon occlusion on haemodynamic function

	Control	Balloon occlusion			Recovery
		7 s	14 s	20 s	
HR	72 (6)	73 (7)	76 (10)	77 (9)*	73 (7)
LVSP (mm Hg)	149 (12)	147 (11)	132 (14)*	125 (9)*	149 (9)
LVEDP (mm Hg)	17 (6)	19 (7)	23 (4)*	29 (7)*	18 (7)
LA "a" (mm Hg)	23 (5)	25 (6)	32 (8)*	41 (3)*	22 (5)
LA "v" (mm Hg)	25 (6)	29 (7)*	39 (5)*	49 (4)*	25 (7)
IVR (ms)	82 (7)	93 (6)*	74 (7)*	70 (4)*	83 (8)
TRT (ms)	130 (9)	145 (8)*	>	>	131 (12)
LV dP/dt _{max} (mm Hg/s)	1453 (219)	1449 (221)	1381 (232)	1299 (229)*	1450 (250)
LV dP/dt _{min} (mm Hg/s)	1570 (230)	1370 (241)*	1197 (230)*	991 (187)*	1610 (240)

* $p < 0.05$ compared with control value (paired t test).

>, greater than previous value, but impossible to measure accurately.

HR, heart rate (beats/min); LVSP, LVEDP, left ventricular systolic and end diastolic pressure respectively; LA "a", LA "v" = "a" and "v" waves in the left atrial pressure trace; IVR, isovolumic relaxation interval; TRT, total relaxation time.

by 16% to 125 (9) mm Hg ($p < 0.05$). Left ventricular end diastolic pressure rose during inflation from 17 (6) mm Hg at baseline to 23 (4) mm Hg after 14 seconds ($p < 0.05$) and to 29 (7) mm Hg after 20 seconds ($p < 0.05$).

At baseline before inflation left ventricular isovolumic relaxation time was 82 (7) ms and peak negative dP/dt (dP/dt_{min}) was 1570 (230) mm Hg/s. Within two to three seconds of LAD occlusion dP/dt_{min} decreased and after five seconds there was deformation of the ascending limb of negative dP/dt. After seven seconds of LAD occlusion the isovolumic relaxation time had lengthened to 93 (6) ms ($p < 0.05$) and dP/dt_{min} had decreased to 1370 (241) mm Hg/s ($p < 0.05$). After nine to 10 seconds of LAD occlusion the isovolumic relaxation time began to shorten again and with periods of ischaemia of 15 to 20 seconds duration it fell to 70 (4) ms (fig 2).

Total left ventricular relaxation time began to lengthen after three seconds of LAD occlusion; 5–6 seconds after occlusion the nadir of the diastolic pressure curve had moved into later diastole producing a diastolic pressure wave that resembled a hammock (fig 2). This pattern of abnormality persisted until the end of LAD occlusion, but with increasing duration of ischaemia it became increasingly dif-

ficult to measure total left ventricular relaxation time accurately.

Within the first five seconds of LAD occlusion there was asynchronous motion of the antero-apicoseptal wall of the left ventricle, with late systolic shortening occurring during the period of isovolumic relaxation. This late inward movement during the rapid filling period of the left ventricular coincided with the notch on the ascending limb of the negative dP/dt signal and may contribute to the impedance to left ventricular filling. There was no rise in left ventricular filling pressure at this point, but the diastolic pressure curve took the hammock-like form described earlier.

Mean left atrial pressure rose within the first seven seconds of LAD occlusion from 13 (5) to 18 (6) mm Hg. The amplitude of the "a" and "v" waves increased from 23 (5) and 25 (6) mm Hg respectively to 25 (6) and 29 (7) mm Hg after seven seconds. After 14 seconds of occlusion the amplitude of the "a" and "v" waves had increased to 32 (8) and 39 (5) mm Hg ($p < 0.05$), and after 20 seconds had increased further to 41 (3) and 49 (4) mm Hg ($p < 0.05$) (fig 3). The greater increase in the "v" wave over the "a" wave was responsible for the significant shortening of isovolumic relaxation time. Maximum left atrial dP/dt rose from 220

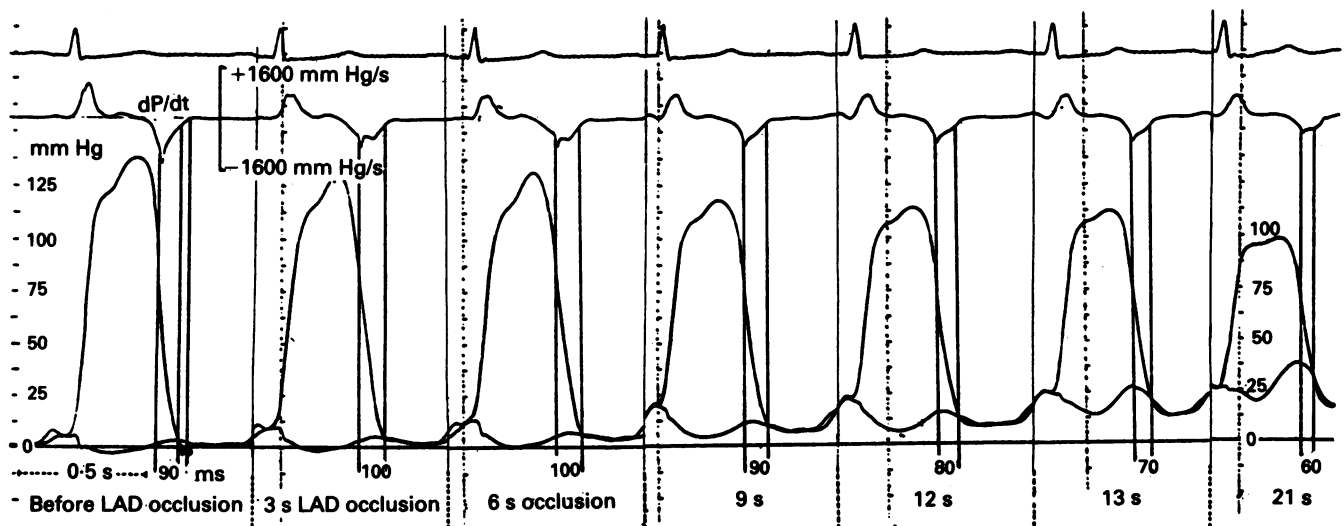


Figure 2 Simultaneous recordings of the electrocardiogram, left ventricular dP/dt and left ventricular and left atrial pressure during LAD occlusion. The isovolumic relaxation time lengthened initially and then shortened as the duration of ischaemia increased (see text). The increase in total relaxation time produced a hammock-like appearance in the diastolic left ventricular pressure trace.

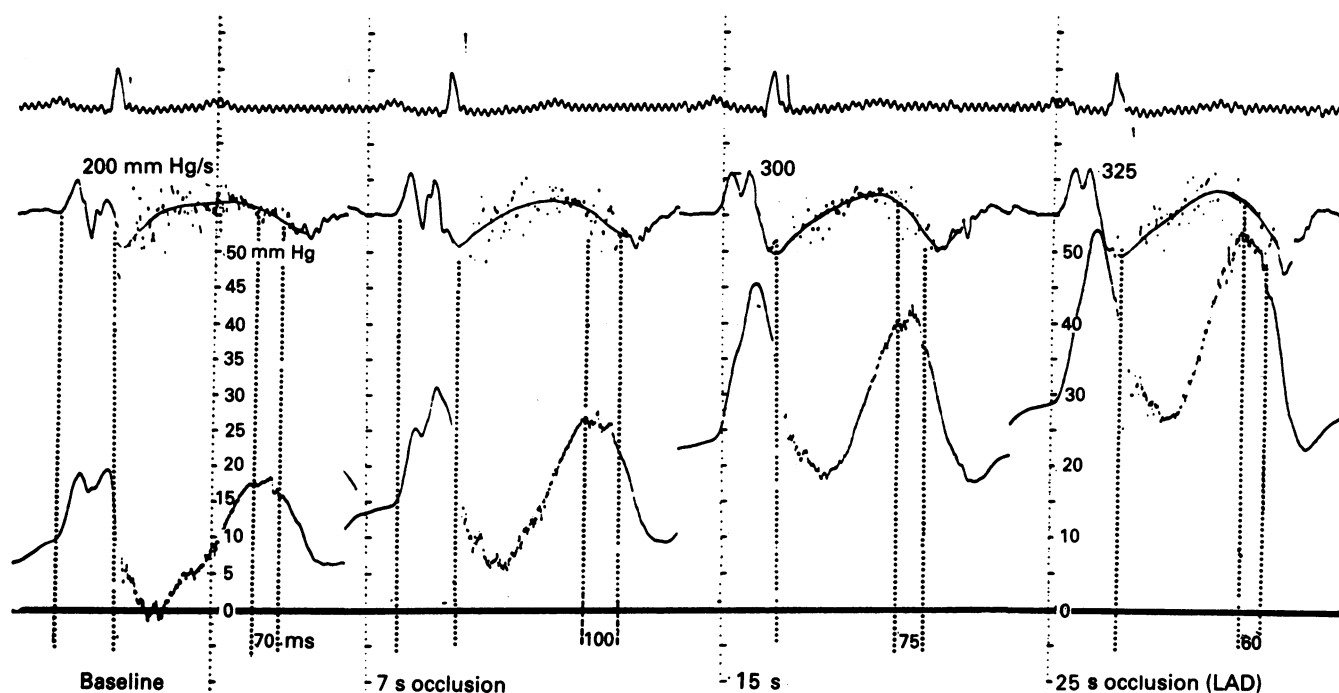


Figure 3 Simultaneous recordings of the electrocardiogram, left atrial dP/dt , and left atrial pressure during LAD occlusion. The greater increase of the "v" wave over the "a" wave was responsible for the earlier crossover of left atrial and left ventricular pressures and the shortening of the isovolumic relaxation time. Atrial dP/dt increased with prolonged ischaemia.

(40) to 350 (20) mm Hg/s during ventricular ischaemia, suggesting increased left atrial contractility.

Ischaemia of the anterior left ventricular wall also affected the systolic function of the ventricle, but later and to a lesser degree. Peak positive dP/dt (dP/dt_{max}) fell slightly throughout the period of balloon inflation from the control value of 1299 (229) mm Hg/s, but the decline did not reach statistical significance until the twentieth second of ischaemia (1299 (229) mm Hg/s, ($p < 0.05$).

Discussion

In the normal heart, left ventricular filling immediately after mitral valve opening is rapid, with a peak transmitral flow rate of 500 ml/s (higher than the rate of flow across the aortic valve during left ventricular ejection). This phase of rapid filling in early diastole lasts about 200 ms and is followed by a phase of slower volume increase (diastasis), the duration of which is dependent on heart rate. The final phase of ventricular filling occurs with atrial systole. Myocardial relaxation, by which the myocardium returns to its original or presystolic (end diastolic) length and tension, is a complex, energy dependent process⁴ which may be the major determinant of the early diastolic filling.⁵ Brutsaert *et al* suggested that it is subject to a triple control mechanism: deactivation, loading, and non-uniformity of load and inactivation in time and space.^{1,2}

The rate of left ventricular relaxation is principally determined by two indices—the maximal rate of left ventricular pressure fall during isovolumic relaxation (dP/dt_{min}) and the time constant of the fall in left ventricular pressure during isovolumic relaxation

(T),⁶⁻¹⁰—but exact measurement of myocardial relaxation is difficult. The peak negative dP/dt is influenced by heart rate, systolic pressure, end systolic volume, and other factors.⁷ The time constant of the left ventricular pressure fall during isovolumic relaxation seems relatively independent of other determinants of cardiac performance, but is a simple mathematical approximation of the pressure decay as a monoexponential function whereas the pressure decay is more complex. The isovolumic fall in left ventricular diastolic pressure during the first 20 seconds of coronary occlusion is not a monoexponential function,¹¹ thus its time constant is of limited usefulness in the study of diastolic function in animals¹¹ or in humans.¹⁰

Nevertheless, assessment of myocardial relaxation is of theoretical importance in the study of acute ischaemia, and mechanical coronary occlusion at the time of coronary angioplasty provides an ideal model. Because there seems to be no single measurement yet described that provides an adequate index of the relaxation process in ventricular myocardium, we used the direct determination of the duration of isovolumic relaxation and the total relaxation time for this purpose. This isovolumic relaxation interval represents the time taken for left ventricular pressure to drop from the level of aortic diastole to that of the left atrium, and is affected by the time course of relaxation as well as by the magnitude of the pressure drop. Relaxation continues after mitral valve opening until the nadir of the left ventricular diastolic pressure, thus total relaxation time is the isovolumic relaxation interval plus the time from mitral valve opening to the lowest point of the left ventricular diastolic pressure curve.

Left ventricular chamber stiffness is a func-

tion of the diastolic pressure-volume relation, and increases with acute ischaemia. However, the pressure-volume relation itself is influenced by several other factors, such as chamber volume and wall thickness, distensibility, composition and viscosity of the myocardium, pericardial function, atrial contraction, pleural pressure, and coronary vascular volume and pressure.¹²

In this study of segmental ischaemia, changes in left ventricular geometry and filling consistent with increasing chamber stiffness were seen during the first few seconds of ischaemia. The isovolumic relaxation time lengthened and the ascending limb of negative dP/dt became notched at the same time as the onset of asynchrony of anteroseptal left ventricular wall motion. The minimum left ventricular diastolic pressure and the point of inflection of the diastolic pressure curve occurred later in diastole, and rapid early filling was reduced by rigidity and delayed relaxation of the anteroseptal wall. Rapid early filling was further impeded by delayed systolic contraction of the anterior left ventricular wall, which was still moving inward when the mitral valve opened.

There was a small, but statistically significant, increase of 12% in the isovolumic relaxation time within the first seven seconds of LAD occlusion. Left ventricular dP/dt_{min} also fell during the first seven seconds of ischaemia, by 13%, but there was no significant change in left ventricular end diastolic pressure or left atrial pressure. With longer periods of ischaemia the left atrial pressure increased and left ventricular and aortic systolic pressures decreased, resulting in earlier opening of the mitral valve and a reduction in the isovolumic relaxation time.

The total left ventricular relaxation time also began to lengthen early after LAD occlusion, with movement of the nadir of the diastolic pressure wave into later diastole, giving a hammock-like appearance to the diastolic pressure curve. The total relaxation time remained prolonged throughout the ischaemic period, which represents relative failure of ventricular relaxation. The rise in left ventricular filling pressure in association with the hammock-like deformation of the diastolic pressure curve indicates a reduction in diastolic left ventricular compliance. The same phenomenon has been reported during experimental coronary occlusion in dogs.¹¹

The effect of reduced diastolic compliance and relative failure of active relaxation of ventricular myocardium is to reduce diastolic filling, particularly the initial phase of rapid early filling. Bonow *et al* showed this phenomenon using radionuclide angiography in patients with coronary artery disease and previous myocardial infarction.¹³

Because the phase of rapid early filling of the left ventricle is impaired during acute ischaemia, the contribution of atrial systole (the

terminal phase of left ventricular filling) must become more important. To examine this, Matsuda *et al* studied the left atrial pressure-volume relation in patients with remote myocardial infarction and in controls.¹⁴ They found that the contribution of atrial systole to left ventricular stroke volume was significantly greater in patients with myocardial infarction than in controls. In the present study we also found augmentation of left atrial performance. Left atrial maximum dP/dt increased significantly, implying an increase in the contractility of left atrial myocardium.

This study shows that percutaneous transluminal coronary angioplasty provides a convenient model for the study of myocardial ischaemia in humans. During regional left ventricular ischaemia left ventricular diastolic function, in particular filling, is impaired before any changes in left ventricular ejection occur. The first manifestation of ischaemia of the ventricular myocardium is asynchronous relaxation, which is followed by prolongation of the time taken for global relaxation. The impairment of left ventricular relaxation and filling is offset to some extent by increased atrial contractility and an increase in the atrial contribution to left ventricular stroke volume.

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